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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,287	05/10/2001	Robert Klein	R00208US (#9	1252

7590 07/15/2002

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,287	KLEIN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' preliminary amendment; IDS, filed 3/21/2001; and second preliminary amendment and supplemental IDS, both filed 6/25/2001.

Specification

1. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

2. The claims are objected to because the lines are crowded too closely together, making reading and entry of amendments difficult. Substitute claims with lines one and one-half or double spaced on good quality paper are required. See 37 CFR 1.52(b).

3. The use of the trademark "Euredur" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

6. Claims 2, 5 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 2, the claim is in improper Markush format. Proper Markush format to be followed in the claim should have the expression "selected from the group consisting of", and only the last two members of the Markush group are separated by the connector operator "and" OR "or". Furthermore, it is unclear to which polymers the claimed ratios of 1:2:1 are referring.

Regarding claim 5, what is the aging inhibitor?

Regarding claims 13 and 14, it is unclear where is the additional PSA layer in relation to the reservoir? Is it attaching the reservoir to the backing or to the skin?

Regarding claim 15, the claim is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. The omitted steps are:

steps for providing therapeutic application in human medicine and steps for controlling the release of the hormone combination.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-9 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of US 5,393,529 ('529), US 5,662,923 ('923), US 5,676,968 ('968), US 5,683,711 ('711), US 5,744,162 ('162), US 5,906,830 ('830) or US 6,153,216 ('216) in combination with any of US 4,954,343 (343) or US 5,951,999 ('999).

US '529 discloses a plaster for controlled release of the active substance consisting of a backing, a pressure sensitive adhesive containing the active substance, and a removable release liner. The pressure sensitive adhesive comprises acrylic acid or methacrylic acid. The active substance is estrogens, such as estradiol, and their derivatives in combination with gestagens, such as norethisterone each in an amount 1-10% (abstract; col.5, lines 35-55). The plaster further comprises a crystallization inhibitor in an amount of 0.1 to 20% wt. (col.3, lines 3-5). The thickness of the adhesive layer may amount from 0.01 to 0.3 mm (col.3, lines 10-12). The pressure sensitive adhesive is in the form of dispersion or hot-melt pressure sensitive adhesive (col.4, lines 13-14, 30-31).

US '923 teaches self adhesive plaster for transdermal application of steroid hormones, comprising a backing layer, an active substance-containing pressure sensitive adhesive layer and detachable protective layer (abstract). The pressure sensitive adhesive layer is hot-melt acrylate adhesive and further comprises polymers, fillers, aging protecting agent (col.2, lines 27-30). The composition comprises polyamides (col.2, line 32). The PSA hot-melt comprises a crystallization inhibitor to stabilize the oversaturated solution of steroid hormones (col.4, lines 15-18). Examples of the hormones are estradiol and norethisterone (col.4, lines 23-48). The PSA hot-melt can be in more than one layer (col.5, lines 24-25).

US '968 discloses a transdermal therapeutic system comprising crystallization inhibitor and penetration enhancer in an active ingredient containing adhesive matrix

such as polyacrylate (abstract; col.4, line 67). The system further comprises a backing and a detachable protective liner (col.1, lines 14-17). The crystallization inhibitors includes polymers and starch derivatives in an amount of 0.1 to 40 % (col.2, lines 1-14, 19-24). The active ingredients are in supersaturated solution and include estradiol and norethisterone in combination, each in an amount of 0.1 to 10 % (col.1, lines 26-30; col.2, lines 50-67; col.3, lines 64-65).

US '711 discloses a transdermal patch comprising estradiol and norethisterone in a supersaturated state in adhesive matrix and the viscosity of the adhesive matrix can inhibit crystallization of the supersaturated adhesive (col.6, lines 31-35; col.8, lines 41-47; col.9, lines 23-25; col.10, lines 52-58). The adhesive comprises acrylate polymers, such as butyl methacrylate and dimethylaminoethyl methacrylate (col.7, lines 50-60; col.8, line 5).

US '162 discloses a plaster comprises a polymer containing the active ingredient in absence of crystallization of the active substances (abstract; col.6, lines 5-6). The polymer comprises acrylic and methacrylic acid and the drug included progesterone and estradiol (col.3, lines 3-16, col.4, lines 35-36). The plaster further comprises antioxidants, aging preventing agents, and fillers (col.5, lines 63-67). The adhesive layer of the plaster has a thickness of 10-1000 micrometer (col.6, lines 15-19).

US '830 discloses a transdermal drug delivery system containing supersaturated drug reservoir of polymeric matrix, contact adhesive or peripheral adhesive ring to affix the reservoir to the skin (abstract; col.3, lines 5-24). The drug is in an amount of 0.1 to

20 % in a polymeric matrix and include estradiol and norethisterone (col.3, lines 40-56; col.7, lines 53-57). The reservoir comprises crystallization inhibitor that includes polymers (col.5, lines 47-49; col.8, lines 14-20). The adhesive matrix is polyacrylate (col.6, lines 64-65).

US '216 discloses a transdermal patch for release of estradiol and progesterone comprises a backing layer, an active ingredient adhesive matrix layer, and a protective release liner (abstract; col.2, lines 47-54). The PSA layer is acrylate copolymers (col.3, lines 66-67). The matrix includes estradiol and norethisterone (NETA) in a supersarurated state. The estradiol is between 0.6 to 1.8 % and the NETA is between 4.0 to 10.0 % (col.4, lines 38-47). The adhesive matrix comprises crystallization inhibitor (col.4, lines 59-60).

The references do not teach the particular crystallization inhibitors disclosed by the applicants. However, the references suggest the inclusion of the crystallization inhibitors of polymers.

US '343 discloses a dermal pharmaceutical preparation comprising a pressure sensitive adhesive comprising methacrylate having an amino group to maintain the drug in a dissolved state and inhibits crystallization (abstract; col.1, lines 30-45). Examples of the amino containing adhesive include methyl methacrylate (col.2, lines 16-34). Examples of the drug to be delivered by this formulation are progesterone and estradiol, used individually or in combination in an amount of 0.1 to 30 % (col.4, lines 21-31, 56-

59). The adhesive layer has a support layer and has a thickness of 5 to 1000 micrometer (col.4, lines 60-67).

US '999 discloses a PSA drug delivery system which reduces the tendency of the hormones to crystallize within the device (abstract; col.1, lines 39-42). The PSA comprises butyl methacylate (col.4, line 10). The device is for delivering hormones such as estradiol and norethisterone (col.7, lines 24-32).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to obtain a transdermal drug delivery device of any of US '529, US 923, US '968, US 711, US '162, US 830 or US '216 comprising steroid hormones and crystallization inhibitor, and replace the crystallization inhibitor by the amino group containing polymers of any of US '343 or US '999 with reasonable expectation of success of stability of the delivery device. Motivation would arise from the teaching of US '343 that he amino containing polymer maintains the drug in dissolved state and provides excellent drug liberation and adhesion to the skin. Motivation would arise from the teaching of US '999 that the adhesive composition comprising methacrylate ester reduces the tendency of hormones to crystallize within the transdermal drug delivery device.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5,353,457 and US 6,238,284 disclosed supersaturated hormone solution in transdermal devices.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Isis Ghali
Examiner
Art Unit 1615

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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